REMARKS

The Office Action and the cited and applied references have been carefully reviewed. No claim is allowed. Claims 1-21 and 28-30 presently appear in this application and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

Claims 22-25 withdrawn from consideration by the examiner are cancelled without prejudice to the filing of a divisional application.

The personal interview among David Karaolis, Allen Yun and Examiners Archie and Navarro on August 4, 2008, is gratefully acknowledged. The undersigned wishes to thank the examiners for the courtesies extended during this interview. The amendments to the claims, as presented in this paper, were discussed with regard to the prior art and enablement rejections. Also discussed was the presentation of experimental results to overcome the enablement rejections, which the examiners indicated would be carefully considered. The arguments and discussions at the personal interview are incorporated into the remarks below.

Claims 1-16 and 28-30 have been rejected under 35 U.S.C. §112, first paragraph, because the examiner states that the specification, while being enabling for a method for attenuating the virulence of a microbial pathogen from *S. aureus* or for inhibiting or reducing colonization by a microbial

pathogen from *S. aureus* in a patient in need thereof, comprising administering to the patient in need an effective amount of c-di-GMP, cGMP and 5'-GMP, does not reasonably provide enablement for any method for attenuating the virulence of a microbial pathogen or for inhibiting or reducing colonization by a microbial pathogen in a patient in need thereof, comprising administering to the patient in need an effective amount of a cyclic dinucleotide analogue thereof. This rejection is respectfully traversed.

The present claims are amended to delete the recitation of "analogue thereof" as discussed at the personal interview.

Furthermore, attached hereto is an executed 1.132 Declaration from David Karaolis presenting experimental results demonstrating that c-di-GMP significantly inhibits microbial colonization, virulence and infection against intranasal (i.n.) or intraperitoneal (i.p.) challenge with various microbial pathogens, including gram positive and grain negative bacteria, a fungal parasite and a viral pathogen. The microbial pathogens used in the experiments span a wide range within the genus of microbial pathogens. Accordingly, one of ordinary skill in the art would readily believe and expect that the presently claimed methods would be applicable to the genus of microbial pathogens and therefore the claims are fully enabled to one of ordinary skill in the art.

In addition, as presented in the attached declaration, various cyclic dinucleotides all showed data that were consistent with the effects observed in the attenuation of virulence and inhibition or reduction of microbial colonization and infection with c-di-GMP. Accordingly, one of ordinary skill in the art is enabled for cyclic dinucleotides, as presently claimed.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 17-21 have been rejected under 35 U.S.C. §112, first paragraph, because the examiner states that the specification, while being enabling for a method for inhibiting *S. aureus* microbial colonization and *S. aureus* biofilm formation or for reducing *S. aureus* colonization and pre-formed *S. aureus* microbial biofilm on a solid surface, comprising exposing the solid surface to an effective amount of c-di-GMP or a cyclic dinucleotide analogue thereof, does not reasonably provide enablement for any method for inhibiting any type of microbial colonization and any type of biofilm formation or for reducing any type of colonization and any type of pre-formed microbial biofilm on a solid surface, comprising exposing the solid surface to an effective amount of a c-di-GMP or any cyclic dinucleotide analogue thereof. This rejection is respectfully traversed.

Claim 17 and 21 are amended to delete the recitation of "analogue thereof" and to recite "bacterial" colonization instead of "microbial" colonization.

Attached hereto is a copy of Mano et al., *ChemMedChem* 2:1410-1413 (2007), which demonstrates that both cyclic dinucleotides, c-di-GMP and c-dGpGp inhibited biofilm formation of three different types of bacteria (gram positive and gram negative), *Pseudomonas aeruginosa*, *Vibrio parahaemolyticus*, and *Staphylococcus aureus*, on a polystyrene solid surface (see page 1410, second full paragraph in right column). These results, while not conducted in the present inventor's laboratory, nevertheless demonstrate that the presently claimed method for inhibiting "bacterial" colonization and biofilm formation is indeed enabled.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 1-8, 10, 13-21 and 28-30 have been rejected under 35 U.S.C. §102(a) as being anticipated by Hook et al., US Patent Application 20020169288 (November 14, 2004). The examiner takes the position that a GehD lipase can be taken to be a cyclic dinucleotide analogue and therefore meets the limitations of the claims. While applicant does not agree with the examiner's interpretation of a cyclic analogue thereof, this issue is obviated by the amendment to the claims to delete the recitation

of "analogue thereof". As the lipase GehD is clearly not a cyclic dinucleotide, Hook cannot anticipate the presently claimed invention.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 1-3, 5-8, 10-11, 13-21 and 28 have been rejected under 35 U.S.C. §102(b) as being anticipated by Costerton et al., US Patent 5,312,813. The examiner takes the position that an antibiotic biocide, such as penicillin, cephalosporins, etc., can be taken to be a cyclic dinucleotide analogue and therefore meets the limitations of the claims. While applicant does not agree with the examiner's interpretation of a cyclic analogue thereof, this issue is obviated by the amendment to the claims to delete the recitation of "analogue thereof". As the antibiotic biocide disclosed in Costerton is clearly not a cyclic dinucleotide, Costerton cannot anticipate the presently claimed invention.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 1-3, 5-11, 13-19, 21 and 28-29 have been rejected under 35 U.S.C. §102(b) as being anticipated by Wooley et al., US Patent Application 20020091074. The examiner takes the position that an antibiotic, such as penicillin, macrolides, etc., can be taken to be a cyclic dinucleotide analogue and therefore meets the limitations of the claims. While applicant

does not agree with the examiner's interpretation of a cyclic analogue thereof, this issue is obviated by the amendment to the claims to delete the recitation of "analogue thereof". As the antibiotics disclosed by Wooley are clearly not cyclic dinucleotides, Wooley cannot anticipate the presently claimed invention.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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